Table 11: **Integrase**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Integrase(20–28)	Pol(762–770)	RAMASDFNL	HIV-1 infection	human(A2 supertype)	[Propato (2001)]
• Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)					
Integrase(22–31)	Pol(764–773)	MASDFNLPPV	HIV-1 infection	human(A2 supertype)	[Propato (2001)]
• Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)					
Integrase(28–36)	Pol(743–751 SF2)	LPPVVAKEI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences – LPPVVAKEI is highly conserved					
Integrase(82–89)	RT(797–804 SF2)	GYIEAEVI	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • GYIEAEVI bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained					
Integrase(89–98)	Pol( )	IPAETGQETA		human(B56)	[De Groot (2001)]
• The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay					

	• IPAETGQETA was newly identified as an HLA-B56 epitope in this study				
Integrase(96–104)	Integrase(823–831)	ETAYFILKL		human(A*6802)	[Dong & Rowland-Jones(1998)]
	• Epitope found in clade A, B, and D – Pers. Comm. S. Rowland-Jones and T. Dong				
Integrase(96–104)	Pol( )	ETAYFILKL	HIV-1 exposed seronegative	human(A*6802)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Integrase(96–104)	Pol( )	ETAYFILKL	HIV-1 infection	human(A*6802)	[Kaul (2001b)]
	• This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls (ML1671)				
Integrase(96–104)	Pol(744–752)	ETAYFILKL	HIV-1 infection	human(A*6802)	[Appay (2000)]
	• This epitope is newly-defined in this study • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV • HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Integrase(96–105)	Pol(744–752)	ETAYFYILKL	HIV-1 exposed seronegative, HIV-1 infection	human(A*6802)	[Kaul (2001a)]
	• ETAYFYILKL cross-reacts with clades A, B and D • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				

- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-A*6802 women, 3/12 HEPS and 9/11 HIV-1-infected women recognized this epitope likelihood ratio 7.9, p value 0.01, and HEPS women tended to respond to DTVLEDINL, while infected women to ETAYFYILKL
- The dominant response to this HLA allele was to this epitope in 2 of the 3/12 HEPS cases and in all 9/11 HIV-1-infected women that responded to the epitope
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV
- Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion
- Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAY-FILKL post-seroconversion

Integrase(127–135)	Pol(869–877)	KAACWWAGI	HIV-1 infection	human(A2 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)

Integrase(173–181)	Pol(888–896)	KTAVQMAVF	human(B*5701)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*5701 epitope
- Epitope is motif based, personal communication from C. Hay

Integrase(173–181)	Pol(888–896)	KTAVQMAVF	human(B57)	[Hay(1999)]

- Epitope is motif based, personal communication from C. Hay

Integrase(177–186)	Pol(919–928)	QMAVFIHNFK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

Integrase(178–186)	Pol(920–928)	MAVFIHNFK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

Integrase(179–187)	Pol(921–929)	AVFIHNFKR	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

Integrase(179–188)	Integrase(179–188 LAI)	AVFIHNFKRK		human(A*1101)	[Brander & Goulder(2001), Fukada (1999)]

- C. Brander notes this is an A*1101 epitope

Integrase(179–188)	Pol(894–903 93TH253 CRF01)	AVFIHNFKRK	HIV-1 exposed seronegative	human(A11)	[Bond (2001)]

- Epitope name: P894-903. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and had been predicted to be a possible A11 epitope using Epimer in [Bond (2001)]

Integrase(219–227)	Pol(934–942 HXB2)	KIQNFRVYY	HIV-1 infection	human(A*3002)	[Mulligan (2001)]
	• Epitope P94 from Patient 11102 with HLA genotypes A*0205, A*3002, B*1402, B*5301, Cw*0802, Cw*0401				
Integrase(219–228)	Pol(919–928)	KIQNFRVYYR	HIV-1 infection	human(A3 supertype)	[Propato (2001)]
	• Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Integrase(241–249)	Pol(576–584)	LLWKGEGAV	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]
	• Slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				
Integrase(241–249)	Pol(956–964)	LLWKGEGAV	HIV-1 infection	human(A2)	[Kundu (1998b)]
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased Env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • LLWKGEGAV is a conserved HLA-A2 epitope included in this study – 6/6 patients had this sequence as their HIV direct sequence, but only four of these had a detectable CTL response				
Integrase(241–249)	Pol(956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human(A2)	[Parker (1992), Parker (1994)]
	• Studied in the context of HLA-A2 peptide binding				
Integrase(241–249)	Pol(956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human(A2)	[Brander (1995)]
	• No CTL activity found in HIV-infected subjects, epitope studied in the context of inclusion in a synthetic vaccine				
Integrase(241–249)	Pol(956–964)	LLWKGEGAW	HIV-1 infection	human(A2, A*0201)	[Ferrari (2000)]
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				